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Albuminuria and Its Relation to Diseases of the Eye

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ATLANTA, GA

Reprint from Ophthalmic Record, September, 1899

ALBUMINURIA AND ITS RELATION TO DISEASES OF THE EYE.*

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The various forms of albuminuria do not bear an equally close relationship to diseases of the eye, but in that connection they all have some interest. Eye diseases, on the other hand, sometimes throw much light on albuminuria and enable us to elucidate the true import of symptoms which might otherwise pass as trifling. Albuminuria, it should be remembered, is of quite common occurrence in the general population. Before its precise frequency among young people was known, when a reaction was setting in some ten to fifteen years ago against the hitherto generally-accepted idea that renal albuminuria always meant serious derangement of the kidney, some were inclined to go to the other extreme and look upon it as lacking in pathological significance in the majority of cases. At this period such names as the "Physiological Albuminuria," the "Albuminuria of Adolescence," "Cyclic Albuminuria," and so on, were applied to the condition, but these carried no explanation with them. With the view of discovering the real frequency of albuminuria in apparently healthy people, I instituted, in 1887, a series of experiments upon the urine of 461 persons. The greatest care was taken to avoid error, and no urine was passed over till I was completely satisfied whether a precipitate were albumen or not. I have no intention of going fully into this matter, an epitome of which can be found in the London *Lancet* (December 10, 1887), along with complete figures in tabular form. But I wish to say a few words which are apropos of my present subject. In one class of 369 boys, in age varying from 12 to 16 inclusive, there were 77 albuminurics, or 20.8 per cent. I desired to find the cause of this. I eliminated George Johnson's cold-bath theory. I proved that it was not produced by food. I found that the urine passed before rising in the morning contained no albumen, but that soon after rising albumen was present, disappearing gradually toward evening. It could be made to disappear at any time by merely causing the patient to lie down, and it would never occur at all throughout the day if he remained recumbent.

*Read before *Georgia State Medical Association*, at Macon.

It will be observed that these experiments were carried on upon the supposition that posture might have something to do with the presence of the albumen. And this was conclusively proved to be the case. Indeed, posture had everything to do with it, for which reason I proposed the name "Postural Albuminuria." This name I find is now in common use by writers in English, German and French journals. There can be little doubt that, as I at first suggested, the albuminuria results from a temporary paresis of the renal vessels, but I by no means wish to be understood as meaning that this albuminuria is truly physiological. I have always held that, as there are of course degrees and kinds of renal lesions, this is merely that stage or form which is of least serious moment, though its ultimate development has not yet been laid bare. A considerable number of these urines were examined microscopically for tube casts, but except once or twice, when hyaline casts were doubtfully present, none were found. In the annual "Lettsomian" lecture last month, in which he makes frequent use of my figures, Dr. Samuel West, the lecturer for the year, remarks that in these cases the albumen is generally serum albumen, and not nuclio-albumen, which latter it is thought by some might come from the urinary passages and not from the kidney, though of this there is no proof whatever. When making my experiments I noticed that a much larger number of the boys who played wind instruments were albuminurics than of those who did not, everything else being the same. The figures were, respectively, 59.4 per cent. and 12.8 per cent.; this I put down to backward pressure. Sir T. Granger Stewart, of Edinburgh University, has since confirmed this observation, though his percentage among band players was not so high as mine. I had a letter some time ago from Dr. Theodore Maxwell, of Woolwich, who is a Russian scholar, informing me that Dr. Weinbaum, of St. Petersburg, had recently examined school boys and had found an even larger percentage than I did, "and among bandsmen in the army his percentage is very high." Dr. Maxwell made an abstract of Dr. Weinbaum's paper for the *Lancet*, but I have never seen it. My observations, to which reference has so far been made, were in connection with adolescents, but at the same time I also as carefully examined 92 other persons at various ages up to 94 and of both sexes. This did not show that adolescence is the period of life most prone to albuminuria; on the contrary it showed that it is more common in middle and still more in advanced age than it is in youth. Dr. West has illustrated by means of a chart my figures in this lecture alongside his own more recent ones (336 persons examined for him by Dr: Levison), and

Mahomed's, showing the proportion of granular to healthy kidneys. Dr. West's and my own agree in gradually ascending till at the ages of 70 or 80 some 70 or 80 per cent of those examined had albuminuria.

It is important to observe that Mahomed's curve remarkably resembles ours. As I have already said, it would be unwise to look upon "physiological" albuminuria as truly physiological. It has not been proven that even in a minority of cases the patients ever get rid of it, and as albuminurics increase with age it is improbable that they do. It indiates a weakness of some kind, and, as West shows from an array of figures from insurance offices, at ages from 20 to 40, as well as over 40, "even a trace of albumen in the urine is of considerable significance. It is more and more likely to mean disease as age advances." We must bear in mind that in granular kidney albuminuria may be scarcely noticeable, and even absent for a time. And this is the form of albuminuria which of all others affects the organs of vision. This suggests how advisable it is in certain eye diseases to make repeated examinations of the urine in the absence of albuminuria and, seeing that the condition of the eye not infrequently first indicates the condition of the kidney, how advisable it also is to have the eyes examined in those cases which suggest albuminuria, but in which it is apparently absent. The most likely time in the twenty-four hours in which to find a urine albuminous is, I may say, in my belief, some three hours after the patient has risen from bed. From what has been said it is evident that in cases of apparently physiological albuminuria it is well to consider even in young people the possibility of the presence of contracting granular kidney. The importance of considering these cases of so-called physiological albuminuria is emphasized by the fact that Eales, who examined the eyes of 14 such cases, young men between 11 and 28, found typical retinal changes in five of them, a sufficiently startling statement. An important question is, "What forms of albuminuria may be accompanied or followed by albuminuric retinitis?" Cases have been reported as dependent upon even amyloid degeneration of the kidney, though these are certainly an exceedingly rare accompaniment of a rare disease, and probably occur only when amyloid degeneration complicates a previously existing granular condition. It is found with the albuminuria of pregnancy, and it is said to be occasionally seen along with the acute parenchymatous nephritis of infectious diseases, such as scarlet fever, as well as the more chronic "large white kidney," but as albuminuric retinitis is certainly peculiarly related to granular renal diseases we must remember that granular kidney may have existed before the acute attack.

The ocular condition may go long undetected, for subjective *symptoms* may, and generally do, remain absent until the case is very far advanced indeed. So long as the macula escapes and the disordered areas are individually of small extent the eye may be yet very seriously diseased before the vision is notably affected. The state of the eye is not infrequently quite unexpectedly discovered, which is often the patient's as well as the physician's first indication of any serious trouble. When vision does become affected it often rapidly goes down hill, though it seldom entirely disappears. The affection is generally binocular, though a number of monocular cases have been reported. I have myself seen only one such. This is mainly a disease of late middle life, but cases are found in youth, even in childhood. These latter seem rather to indicate a dependence upon congenital syphilis. It is not really known in what proportion of cases of granular kidney albuminuria develops, though various statements have been made. The ophthalmoscopic picture of typical retinitis albuminurica ought to be of interest to all practitioners of medicine, because it reveals to the eye in the living body pathological changes which may be more marked in the retina than in other tissues, its vascular supply being terminal, without anastomoses, but is illustrative of lesions present in other and more vital organs, such as brain and kidney. These visible ocular changes have been best described by Marcus Gunn, but I shall place them under five heads. One or other of them usually predominates, though they may all be present at the same time. They are: (1) vascular changes, (2) hemorrhages, (3) white spots, (4) exudations, (5) neuritis.

(1) The pathological condition, which, if not always noticeable, yet probably underlies all the others, is the change in the vessels. This change is made up of an apparent narrowing in the size of the arteries compared to the veins, the broadening of their light streak, their tortuosity, the disappearance of such part of a vein crossing beneath an artery as is covered by the walls of that artery, which, though another explanation has been given, seems to show that these walls are opaque, as does their visibility when lying beneath a vein; occasional local fusiform swellings on some of the smaller arteries, and distension of veins with loss of central light streak from compression by thickened arteries crossing them.

The morbid anatomy to which these changes are due consists in a thickening and degeneration of the walls of the arteries in each of their coats, but especially the intima, frequently hyaline in appearance, but not giving the chemical reaction of amyloid degeneration, and sometimes so

marked as to produce total obliteration of the lumen on the one hand, and permit of aneurismal dilatation on the other. Even the capillaries may be so much affected as to remain open on division. These appearances are not confined to the retina, but are found in all the vascular parts of the eye. In the rare cases originating with acute infectious diseases, of which I personally cannot recall an example, it may be that the renal and ocular lesions are synchronous in their beginning, but it is most probable that in cases of granular kidney the renal pathology precedes that of the eye, and that the latter results from abnormal and irritating constituents of the blood in spite of those cases in which the ocular affection has been observed before albuminuria was discovered.

(2) Hemorrhages, as might be expected from such vessels, are frequent. They are generally minute, but may be so large as to fill the vitreous chamber. Occasionally hemorrhagic glaucoma follows in their wake. It is not unlikely that in some cases thrombosis is present. The bleeding is most frequently from veins or capillaries, but may also come from arteries, and may be in any part of the fundus. It is more frequently toward the vitreous aspect of the retina in the nerve-fiber layer, whose anatomical arrangement then gives it a flame-shaped appearance, than in the deeper layers in which it is more circular. Hemorrhages may gradually become absorbed.

(3) The white spots, though actually preceded by disease of the vessels, are yet very frequently the first visible lesion. They are usually quite small, are situated toward the vitreous aspect of the retina in the region of the macula, and very often between it and the disc. They very commonly form lines like the spokes of a wheel, radiating from the yellow spot. They are somewhat chalky in appearance, but may be bright and glistening. The spots, which, when brilliant, contain cholestrin, are produced by the fatty degeneration of nerve and fibrous tissue as well as of old exudations. The radiation round the macula has been said to result from the degeneration of the fibers of Mueller, which there, instead of being vertical, run obliquely in the retinal tissue and thus present their length rather than merely their ends to view; but according to Marcus Gunn the lines arise from folding of the retina by œdema. The region of the macula contains neither arteries or veins, and this should be remembered when considering its special liability to degeneration. These spots are seldom, in cases of granular kidney, seen to disappear.

(4) The state of the vessels, along with the increased blood pressure incident to the renal affection, constitutes a condition of things in which

exudations are a certainty. Œdema affects other tissues of the eye as well as the retina and replaces the normally distinct outlines of the fundus by a delicate grayish cloudiness. Lymph may exude in places and give rise to white spots, which may be confused with the spots of degeneration already described, but they are less defined in outline, may be raised above the normal level of the retina and are woolly in appearance. It is these white spots which are liable to change in position, to diminish in intensity, and even to disappear. Serous exudations behind the retina not infrequently separate it from the choroid. These detachments tend to be peripheral and symmetrical in both eyes. In cases due to pregnancy they sometimes disappear by reattachment on absorption of the exudation. Occasionally detachments are hemorrhagic in origin. The microscope shows the retinal tissues separated by spaces filled with fluid, while the rods and cones are apt to be swollen, though they may be normal.

(5) Swelling of the optic disc with blurring of its edges is common, and sometimes this may be excessive and bear a close resemblance to the "choked disc" of cerebral tumors, which resemblance may be intensified by the presence of vomiting and headache. The usual signs of secondary atrophy are liable to appear at a later date.

The *prognosis* in albuminuric retinitis depends upon the disease accompanying it. When due to removable causes, such as pregnancy, the ocular lesions may cease with their cause. It is in chronic renal disease, especially granular kidney, that albuminuric retinitis appears as one of the most certain indications that the final stages of the patient's life have arrived. Vision, indeed, may all through continue fairly good, though it is liable gradually or suddenly to become seriously involved or even lost, but it is as an indication of his approaching end that in these cases that albuminuric retinitis has its chief importance. If the patient lives for 24 months after its discovery he survives beyond the average time, for many die within a very few months. Cases have been recorded, however, of the prolongation of life to several, even to 12 years. This depends, of course, somewhat on the period of its discovery and upon the patient's circumstances. The wealthy classes, who can choose their environment, are known to live longer than the poor.

There is not time to consider the *diagnosis*, which, however, rarely presents difficulties. I *have* seen it hard to say whether the ocular appearances were due to renal mischief or to a cerebral tumor, and this has been the experience of others. Between albuminuric retinitis and that associated with diabetes the ophthalmoscope can really make no proper dis-

tinction. Diabetic cases are not infrequently also albuminuric, and it should be borne in mind that, though kidney changes are undoubtedly secondary and variable in kind and degree, they are always present. These consist of one or more of the following: Enlargement and fatty degeneration; contraction of the whole organ and thinning of its cortex; not uncommonly all the histological appearances of granular kidney; hyaline transformation of the epithelium of Henle's tubes; tubercle, lardaceous, disease, and even gangrene have been found.

The *treatment* is that for the disease preceding the ocular affection and, without going into particulars, may almost be summed up in the words purgation, diaphoresis, climate and hygiene.

While, in the short time properly allowed for these papers, we naturally, when dealing with the relation of albuminuria to eye diseases, consider first and chiefly albuminuric retinitis, it would be a great oversight to omit entirely those others which are equally closely related to it and are indeed dependent upon the same cause. I shall in closing say merely a few words concerning them. They may very well be divided into those which depend upon lesions of the visual apparatus: *first*, outside the brain (among which is of course albuminuric retinitis itself), and *second*, within the brain. Among the former œdema and hemorrhage in the lids and conjunctiva, hemorrhage into the optic nerve and into the orbit. Embolism or thrombosis of the central vessels of the retina is probably less uncommon than has been supposed. Iritis and cataract are probably little, if any, more common in albuminurics than in the general population.

Among intra-cranial lesions hemorrhage into the nuclei or trunks of the nerves supplying them has been said to produce temporary paralysis of some of the external muscles of the eye. Uræmic amblyopia is more frequently met with. It is probably the result of extreme cerebral anæmia due to vascular contraction caused by the irritation of poisonous matters in the circulation. The resulting blindness usually affects both eyes, and may be incomplete and transient, or absolute vision returning only after some hours' duration, though it may be delayed for three or four days. The pupils generally react to light, which indicates the cortical origin of the attack, but occasionally they do not, and then the nerve or optic ganglia are involved. In these latter cases the optic disc is likely to be found swollen. When recovery of vision does not fully take place there must be some organic lesion, and post-mortem examinations have shown that apparently functional cases have sometimes had their origin in small hemorrhages. It should also be noted that central amblyopia is not infrequently accompanied by other nerve symptoms, such as hemiplegia.